UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,671	08/09/2001	Bo Arthur Einar Tjellstrom	11133Z	3329

7590 06/02/2003

SCULLY, SCOTT, MURPHY & PRESSER
400 Garden City Plaza
Garden City, NY 11530

EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	9

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/925,671	Applicant(s) TJELLSTROM ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on *14 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7,8* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Claims 1-12 are pending.

2. Applicant's election with traverse of a species of composition administered in the instant methods that comprises at least about 25% IgG in Paper No. 6 is acknowledged. The traversal is on the ground that other Ig preparations are also suitable for use in the instant methods. Applicant's argument is not found persuasive because although multiple Ig preparations may be used in the instant methods, as previously noted each Ig preparations comprising varying amounts of individual immunoglobulin isotypes are distinct.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10 as they read on the elected species are under consideration in the instant application.

Claims 11-12 are withdrawn from consideration because Applicant has identified the elected species as a method comprising any pooled human polyclonal immunoglobulin preparation that comprises at least about 25% IgG, but has placed no limitation on the presence or absence of other isotypes or their relative amounts.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) and 120 is acknowledged. However, neither provisional application 60/074,193 nor parent application USSN 09/247,396 upon which priority is claimed provides clear support under 35 U.S.C. 112 for the instant claims.

In particular, it is unclear if the "pooled human polyclonal immunoglobulin preparation" recited in the instant claims is adequately supported by the "human immunoglobulin preparation" disclosed in the priority applications.

Applicant is invited to point to adequate written support for the above noted limitation.

However at present it appears that the effective filing date of the instant claims is the filing date of the instant application, i.e., August 9, 2001.

Specification

4. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

The use of various trademarks has been noted in this application. Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections – 35 U.S.C. §§ 102 and 103

5. The following rejection under 35 USC 102 is set forth under the assumption that the effective filing date of the instant claims is that of the instant application, i.e., August 9, 2001.

It is noted that should adequate written support be established for the claimed limitations in USSN 09/247,396 and provisional application 60/074,193, Tjellstrom et al. (Acta Paediatr 1997; 86:221-223) would not be available as prior art. The statement by the publisher provided in parent application USSN 09/247,396 that Tjellstrom et al. was not mailed until, at the earliest, Feb 11, 1997 has been made of record in the instant file.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 3-7 and 9-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Tjellstrom et al. (Acta Paediatr 1997; 86:221-223) as evidenced by Eibl and Wolf (in "Therapeutic Immunology", eds Austen et al., 1996 Blackwell Sciences, Inc., Cambridge, Massachusetts, Chapter 22 "Immunoglobulin A", pages 297-310) and the instant disclosure on page 10 at lines 29-31 stating that IgAbulin is an appropriate commercial immunoglobulin preparation for use in the instant methods.

Tjellstrom et al. teach a method of treating the inflammatory bowel disease Crohn's disease by orally administering to a patient a preparation of immunoglobulin that is IgAbulin (see entire document, especially page 221, 1st paragraph). Crohn's disease is an example of an inflammatory bowel disease involving mucosal inflammation.

Tjellstrom et al. teach that IgAbulin comprises 90mg of immunoglobulin per ml, of which 60 mg is IgA (page 221, 1st paragraph); therefore the immunoglobulin in IgAbulin is at least one of IgA or a mixture of IgA. Tjellstrom et al. teach that 14 mL of IgAbulin was administered in each dose, three times daily (e.g., Case 1). Since the immunoglobulin concentration in IgAbulin was 90 mg/mL and 14 mL were administered per dose, the immunoglobulin was administered in a dose of 1.26 grams at least once a day. Tjellstrom et al. teach that the IgAbulin was administered to a patient, and so must necessarily have been formulated in a pharmaceutically acceptable carrier (see e.g., Case 1).

Although Tjellstrom et al. is silent as to the concentration of IgG in the preparation. Eibl and Wolf state that IgAbulin is about 70% IgA and 25% IgG (page 304, right column, middle of 2nd paragraph).

Further, the specification discloses on page 10 at lines 29-31 that IgAbulin is a commercial immunoglobulin preparation appropriate for use in the instant methods. Thus IgAbulin must be a pooled human polyclonal immunoglobulin preparation.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the IgAbulin administered to treat Crohn's disease.

The reference teachings thus anticipate the instant claimed invention.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hassig (U.S. Pat. No. 4,676,982) and Hardie (U.S. Pat. No. 4,477,432, IDS).

The claims are drawn to a method of treating inflammatory bowel disease, including ulcerative colitis and Crohn's disease, by orally administering to a patient a pooled human polyclonal immunoglobulin preparation comprising at least about 25% IgG.

Hassig teaches and claims a method of treating chronic inflammatory diseases of the bowel, including ulcerative colitis and Crohn's disease, by intravenously administering an effective dose of polyvalent immunoglobulin (see entire document, e.g., Abstract and claims).

Hassig teaches that the immunoglobulin preparation is intact IgG obtained from blood serum fractions (i.e., is a pooled human polyclonal immunoglobulin preparation, see column 1, especially lines 32-48).

An IgG preparation is necessarily at least about 25% IgG polyclonal antibodies.

Hassig differs from the instant method by not teaching oral administration and the doses and formulations for oral administration.

However, Hardie teaches that immunoglobulin preparations prepared for intravenous administration could also be administered orally without a loss of therapeutic efficacy (see entire document).

Hardie teaches that oral administration of Ig, including IgG, has advantages over parenteral (including intravenous) administration because oral administration avoided the pain of an injection, by provided an easy means of administering the composition, and provided an administration route by which larger doses could be administered if needed (see column 2, especially "Summary of the Invention").

Hardie teaches formulating the oral immunoglobulin preparation as part of a pharmaceutically acceptable carrier, and teaches encapsulation of the composition, which would provide an enteric coating (see columns 3-4.

Hardie teaches that the formulation administered in the examples of the invention for treatment of enteric infection contained 14 mg/dl (1.4 mg/mL) of IgG and that 1-8 mL/kg/day was administered (1.4-11.2 mg/kg). Thus for an adult of 70 kg, the corresponding dose would be 98-784 mg, which falls within dosage recited in instant claim 7.

The ordinary artisan at the time the invention was made would therefore have found it obvious to administer the IgG preparation taught by Hassig for the treatment of inflammatory bowel disease by the oral route, using pharmaceutically acceptable carriers appropriate for oral administration. Both Crohn's disease and ulcerative colitis are examples of inflammatory bowel disease involving mucosal inflammation. The ordinary artisan would have been motivated to substitute oral administration for intravenous administration because Hardie teaches that oral administration is advantageous compared to parenteral, including intravenous, administration. Finally, given the teachings of Hardie that orally administered immunoglobulin preparations, including IgG preparations, could be administered orally without loss of function for the treatment of other enteric diseases, the ordinary artisan at the time the invention was made would have had a reasonable expectation that oral administration would also be effective in the methods taught by Hassig. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. Claims 1- 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tjellstrom et al. (Acta Paediatr 1997; 86:221-223) as evidenced by Eibl and Wolf (in "Therapeutic Immunology", eds Austen et al., 1996 Blackwell Sciences, Inc., Cambridge, Massachusetts, Chapter 22 "Immunoglobulin A", pages 297-310) and the instant disclosure on page 10 at lines 29-31 stating that IgAbulin is an appropriate commercial immunoglobulin preparation for use in the instant methods; in view of Hassig (U.S. Pat. No. 4,676,982).

The claims are drawn to a method of treating inflammatory bowel disease, including ulcerative colitis and Crohn's disease, by orally administering to a patient a pooled human polyclonal immunoglobulin preparation comprising at least about 25% IgG wherein the immunoglobulin is enterically coated.

Tjellstrom et al. as evidenced by Eibl and Wolf and the disclosure on page 10 at lines 29-31 have been discussed supra and teach a method of treating the inflammatory bowel disease Crohn's disease by orally administering to a patient a preparation of immunoglobulin that is IgAbulin (see entire document, especially page 221, 1st paragraph).

Tjellstrom et al. do not teach a method of treating ulcerative colitis, nor that the immunoglobulin is enterically coated.

Hassig teaches that both ulcerative colitis and Crohn's disease can be treated by intravenously administering an effective dose of polyvalent immunoglobulin (see entire document, e.g., Abstract and claims).

Therefore, it would have been obvious to the ordinary artisan at the time the invention was made that the method taught by Tjellstrom for oral treatment of Crohn's disease by administering an immunoglobulin composition could also be used for treating the related inflammatory bowel disease of ulcerative colitis. Both Crohn's disease and ulcerative colitis are examples of conditions involving mucosal inflammation. In view of the teachings of Hassig that both Crohn's disease and ulcerative colitis cold be treated by intravenous administration of immunoglobulin, and the teachings of Tjellstrom et al. that Crohn's disease could also be treated orally, the ordinary artisan would also have had a reasonable expectation that oral therapy as taught by Tjellstrom could also be used to treat ulcerative colitis. The ordinary artisan would have been motivated to treat ulcerative colitis to provide therapeutic relief to patients suffering from ulcerative colitis.

Finally, it would also have been obvious to the ordinary artisan at the time the invention was made to formulate any composition for oral administration with an enteric coating. Enteric coatings were well known in the art at the time the invention was made and improved the delivery of compounds targeted for delivery to the gut. Thus the ordinary artisan would both have been motivated to utilize an enteric coating to improve delivery to the gut, and would have had a reasonable expectation that the immunoglobulin could be dried and formulated with an enteric coating. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
May 29, 2003

PHILLIP GAMBEL

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
5/30/03